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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,178	02/28/2005	Raman Kumar Bakshi	21140YP	6470

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MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	**PAPER NUMBER**
1624	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,178	BAKSHI ET AL.	
	Examiner	Art Unit	
	/Venkataraman Balasubramanian/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27,29-32 and 37-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27,29-32 and 37-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/6/2005 & 7/17/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment, which included cancellation of claims 28, 33-36, 41-46 and amendment to claims 27, 30, 31 and 40, filed on2/28/2005, is made of record.

Claims 1-27, 29-32 and 37-40 are now pending.

Information Disclosure Statement

References cited in the Information Disclosure Statements, filed on 6/6/2005 & 7/17/2006, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25, 27 and 40 are rejected under U.S.C. 112, first paragraph, because the specification while being enabling for treating diabetes and obesity does not reasonably provide enablement for treatment, control, or prevention of any or all disorders, diseases or conditions responsive to the activation of the melanocortin-4 receptor as well as treating and preventing an obesity-related disorder selected from the group consisting of overeating, binge eating, and bulimia, hypertension, diabetes, elevated plasma insulin concentrations, insulin resistance, dyslipidemias, hyperlipidemia, endometrial, breast, prostate and colon cancer, osteoarthritis, obstructive sleep apnea, cholelithiasis, gallstones, heart disease, abnormal heart rhythms and arrythmias, myocardial infarction, congestive heart failure, coronary heart

disease, sudden death, stroke, polycystic ovary disease, craniopharyngioma, the Prader-Willi Syndrome, Frohlich's syndrome, GH-deficient subjects, normal variant short stature, Turner's syndrome, metabolic syndrome, insulin resistance syndrome, sexual and reproductive dysfunction, infertility, hypogonadism, hirsutism, obesity-related gastro-esophageal reflux, Pickwickian syndrome, cardiovascular disorders, inflammation, systemic inflammation of the vasculature, arteriosclerosis, hypercholesterolemia, hyperuricaemia, lower back pain, gallbladder disease, gout, and kidney cancer, cardiac hypertrophy and left ventricular hypertrophy. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims.

The instant method of use claims 26, 27 and 40, are drawn treatment, control, or prevention of any or all disorders, diseases or conditions responsive to the activation of the melanocortin-4 receptor. Instant claims, as recited, are reach through claims. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the inhibition of kinase by the instant compounds, instant claims reaches through by inhibiting melanocortin-4 receptor melanocortin-4 receptor and thereby treating, controlling and preventing any or all diseases in general and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as inhibitor of melanocortin-4 receptor, based on limited assay, it is claimed that treating, controlling and preventing any or all diseases in general, for which there is no enabling disclosure. The scope of the claims also includes various diseases such as treating and preventing an obesity-related disorder selected from the group consisting of overeating, binge eating, and bulimia, hypertension, diabetes, elevated plasma insulin concentrations, insulin resistance, dyslipidemias, hyperlipidemia, endometrial, breast, prostate and colon cancer, osteoarthritis, obstructive sleep apnea, cholelithiasis, gallstones, heart disease, abnormal heart rhythms and arrythmias, myocardial infarction, congestive heart failure, coronary heart disease, sudden death, stroke, polycystic ovary disease, craniopharyngioma, the Prader-Willi Syndrome, Frohlich's syndrome, GH-deficient subjects, normal variant short stature, Turner's syndrome, metabolic syndrome, insulin resistance syndrome, sexual and reproductive dysfunction, infertility, hypogonadism, hirsutism, obesity-related gastro-esophageal reflux, Pickwickian syndrome, cardiovascular disorders, inflammation, systemic inflammation of the vasculature, arteriosclerosis, hypercholesterolemia, hyperuricaemia, lower back pain, gallbladder disease, gout, and kidney cancer, cardiac hypertrophy and left ventricular hypertrophy which is not adequately enabled solely based on the activity of the compounds provided in the specification. The instant compounds are disclosed to have inhibitor of melanocortin-4 receptor activity and it is recited that the instant compounds are therefore useful in treating any or all diseases stated above for which applicants provide no competent evidence. It appears that the applicants are asserting

that the embraced compounds because of their mode action as above said inhibitor that would be useful for all sorts of diseases such as autoimmune diseases, any inflammation or any disease which involve signal transduction pathway. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Moreover many if not most of diseases such as psoriasis and cancers, autoimmune diseases are very difficult to treat and despite the fact that there are many drugs, which can be used for "inflammatory condition".

No compound has ever been found to treat diseases of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. Different types of diseases affect different organs and have different methods of harm to the body. Thus, it is beyond the skill of clinician today to get an agent to be effective against all diseases generally.

In addition scope of the claim 40 includes prevention. To prevent" actually means to anticipate or counter in advance, to keep from happening etc. (as per Websters II Dictionary) and there is no disclosure as to how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the inflammatory and or immune disease(s) or disorder(s) claimed herein.

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Cody et al., Hum. Genet., 105:426-427, 1999 and Schioth et al., Regulatory Peptides, 106, 7-12, 2002.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating , controlling and preventing any or all treating any or all diseases, disorders and conditions responsive to the activation of the melanocortin-4 receptor.

2) The state of the prior art: A publication expressed that the melanocortin-4 receptor inhibition effects are unpredictable and are still exploratory. See Cody et al., and Schioth et al. cited above.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating, controlling and preventing any or all condition by the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all condition and the state of the art is that the effects of melanocortin-4 receptor inhibitors are unpredictable.

6) The breadth of the claims: The instant claims embrace treating, controlling and preventing any or diseases with a large genus of compounds.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical

nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was 'filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 8-10, 14-16, 26, 29, 30 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Gante et al., DE 19713000.

Gante et al., teaches several hetero-substituted piperazine compounds for treating arteriosclerosis, which include instant compounds, composition and method of use. See page 2, formula I and note when Het is pyridyl or piperidyl, X is N and B is the

fourth choice, the compounds taught by Gante et al., include instant compounds. See pages 2--8 for details of the preferred embodiments and process of making these compounds. Particularly, see page 6 for such a choice as preferred embodiment. See pages 8-12 for examples of compounds made. Especially see examples 2 and 3 .

Claims 1, 5, 8-10, 14-16, 26, 29, 30 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Rudolf et al., US 6,344,449. CA 128:197358, 1998. CA Plus Abstract also provided.

Rudolf et al., teaches several piperazine compounds useful as neurotransmitter which include instant compounds, composition and method of use. See column 1, formula I and note the given definition of all variable groups, the compounds taught by Rudolf et al., include instant compounds. See column 2-32 for details of the preferred embodiments and process of making these compounds. Particularly, see column 32-64 for various species made. Note various piperidinecarbonyl and piperazinecarbonyl compounds are taught therein. See entire document. Especially see examples 269 and 275. See CAPLUS Abstract.

Claims 1, 5, 8-10, 14-16, 26, 29, 30 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Morriello et al., US 5,721,250.

Morriello et al., et al., teaches several piperidine compounds useful for treating obesity which include instant compounds, composition and method of use. See column 2, formula I and note the definition of all variable groups. With these definition, the compounds taught by Morriello et al., include instant compounds. See column 2-24 for details of the preferred embodiments. Particularly, see column 18 for various urea

species. See column 27-31 for process of making these compounds. See entire document. Especially see column 148, entry 8 and 9.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5, 8-10, 14-16, 26, 29, 30 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over et al., Gante et al., DE 19713000.

Teachings of Gante et al., as discussed in the above 102 rejection is incorporated herein. As noted above, Gante et al., teaches several hetero-substituted piperazine compounds for treating arteriosclerosis, which include instant compounds, composition and method of use. See page 2, formula I and note when Het is pyridyl or piperidyl, X is N and B is the fourth choice, the compounds taught by Gante et al., include instant compounds. See pages 2--8 for details of the preferred embodiments and process of making these compounds. Particularly, see page 6 for such a choice as preferred embodiment. See pages 8-12 for examples of compounds made. Especially see example 2 and example 3 .

Instant claim 28 differs from Gante et al., in requiring various choices of R^2 besides pyridyl. Although Gante et al. include piperidyl , Gante et al., does not exemplify all the compounds of subgenus with Het as piperidyl.

However, Gante et al., teaches equivalency of the compounds taught in pages 8-12 with those generically claimed in page 2.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make various compounds of formula I using teachings of Gante et al., and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Claims 1-27, 29-32 and 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rudolf et al., US 6,344,449.

Teachings of Rudolf et al., as discussed in the above 102 rejection is incorporated herein. As noted above, Rudolf et al., teaches several piperazine compounds useful as neurotransmitter, which include instant compounds, composition and method of use. See column 1, formula I and note with given the definition of all variable groups, the compounds taught by Rudolf et al., include instant compounds. See column 2-32 for details of the preferred embodiments and process of making these compounds. Particularly, see column 32-64 for various species made. Note various piperidinecarbonyl and piperazinecarbonyl compounds are taught therein. See entire document. Especially see examples 269 and 275. See CAPLUS Abstract.

Instant claim 28 differs from Rudolf et al., in requiring various choices of R^1, R^2 and other variable groups. Although Rudolf et al. include all such choices in the variable group definition of formula shown in column 1, Rudolf et al., does not exemplify all the compounds of subgenus piperazinyl carbonyl. However, Rudolf et al., teaches large number of such variation with piperidinyl carbonyl compounds .In addition Rudolf et al., teaches equivalency of the compounds taught in column 32-64 with those generically claimed in column 1.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make various compounds of formula I using teachings of Rudolf et al., and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Claims 1-27, 29-32 and 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morriello et al., US 5,721,250.

Teachings of Morriello et al., as discussed in the above 102 rejection is incorporated herein. As noted above, Morriello et al., teaches several piperidine compounds useful for treating obesity which include instant compounds, composition and method of use. See column 2, formula I and note the definition of all variable groups. With these definition, the compounds taught by Morriello et al., include instant compounds. See column 2-24 for details of the preferred embodiments. Particularly, see column 18 for various urea species. See column 27-31 for process of making these compounds. See column 47-150 for various compounds made. . Especially see column 148, entry 8 and 9.

Instant claim 28 differs from Morriello et al., in requiring various choices of R^1, R^2 and other variable groups. Although Morriello et al., include all such choices in the variable group definition of formula shown in column 2, Morriello et al., does not exemplify all the compounds of subgenus piperazinyl carbonyl. However, Morriello et al., teaches large number of such variation with hetero carbonyl compounds .In addition Rudolf et al., teaches equivalency of the compounds taught in column 47-150 with those generically claimed in column 1.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make various compounds of formula I using teachings of Morriello et al., and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

Venkataraman Balasubramanian

6/24/2007